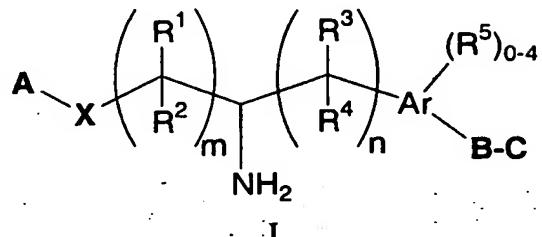


WHAT IS CLAIMED IS:

1. A compound represented by Formula I:



or a pharmaceutically acceptable salt or hydrate thereof, wherein:

Ar is phenyl or naphthyl;

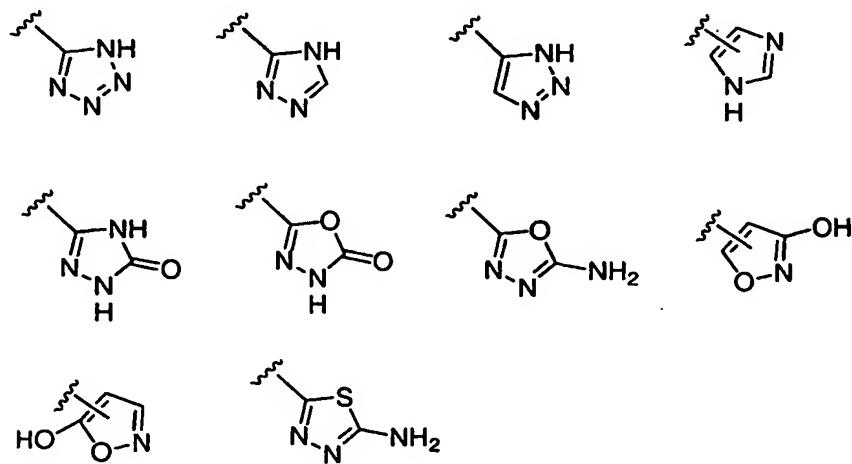
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$m = 1, 2, 3, \text{ or } 4;$

$n = 0, 1, 2, 3, \text{ or } 4;$

15 X is a bond, O, NH or S(O)_k, wherein k is 0, 1 or 2;

A is selected from the group consisting of: $-\text{CO}_2\text{H}$, $-\text{PO}_3\text{H}_2$, $-\text{PO}_2\text{H}_2$, $-\text{SO}_3\text{H}$, $-\text{PO}(\text{R}_8)\text{OH}$,



each R¹ is independently selected from the group consisting of: hydrogen, halo, hydroxy, -CO₂H, C₁-4alkyl, C₁-4alkoxy, C₁-4alkylthio and aryl, wherein said C₁-4alkyl, C₁-4alkoxy and C₁-4alkylthio are each optionally substituted from one up to the maximum number of substitutable positions with halo and wherein said aryl is optionally substituted with 1-5 substituents independently selected from halo and C₁-4alkyl, or

when m is 2, 3, or 4, two R¹ groups on adjacent carbon atoms may be joined together to form a double bond;

each R³ is independently selected from the group consisting of: hydrogen, halo, hydroxy, -CO₂H, C₁-4alkyl, C₁-4alkoxy, C₁-4alkylthio and aryl, wherein said C₁-4alkyl, C₁-4alkoxy and C₁-4alkylthio are each optionally substituted from one up to the maximum number of substitutable positions with halo and wherein said aryl is optionally substituted with 1-5 substituents independently selected from halo and C₁-4alkyl, or

when n is 2, 3, or 4, two R³ groups on adjacent carbon atoms may be joined together to form a double bond;

R² and R⁴ are each independently selected from the group consisting of: hydrogen, halo, hydroxy, -CO₂H, C₁-4alkyl, C₁-4alkoxy, C₁-4alkylthio and aryl, wherein said C₁-4alkyl, C₁-4alkoxy and C₁-4alkylthio are each optionally substituted from one up to the maximum number of substitutable positions with halo and wherein said aryl is optionally substituted with 1-5 substituents independently selected from halo and C₁-4alkyl;

or R¹ and R² or R³ and R⁴ residing on the same carbon atom may optionally be joined together to form a carbonyl group,

each R₅ is independently selected from the group consisting of: halo, aryl, C₁-6alkyl, C₃-6cycloalkyl, C₁-6alkoxy, C₁-6alkylthio and C₃-6cycloalkoxy, said C₁-6alkyl, C₃-6cycloalkyl, C₁-6alkoxy, C₁-6alkylthio and C₃-6cycloalkoxy optionally substituted

5 from one up to the maximum number of substitutable positions with halo,

R₈ is selected from the group consisting of: C₁-4alkyl and aryl, wherein said C₁-4alkyl is optionally substituted with 1-3 halo groups and aryl is optionally substituted with 1-5 substituents independently selected from the group consisting of: halo, C₁-6alkyl, C₃-6cycloalkyl, C₁-6alkoxy, C₁-4alkylthio and C₃-6cycloalkoxy, said C₁-6alkyl, C₃-6cycloalkyl, C₁-6alkoxy, C₁-4alkylthio and C₃-6cycloalkoxy optionally substituted from one up to the maximum number of substitutable positions with halo,

C is selected from the group consisting of:

15 (1) C₁-8alkyl, C₁-8alkoxy, -(C=O)-C₁-6alkyl or -CHOH-C₁-6alkyl, said C₁-8alkyl, C₁-8alkoxy, -(C=O)-C₁-6alkyl and -CHOH-C₁-6alkyl optionally substituted with phenyl, and

20 (2) phenyl or HET, each optionally substituted from one up to the maximum number of substitutable positions with a substituent independently selected from the group consisting of: halo, phenyl, C₁-4alkyl, C₁-4alkoxy and aralkyl, said C₁-4alkyl and C₁-4alkoxy groups optionally substituted from one up to the maximum number of substitutable positions with a substituent independently selected from halo and hydroxy, and said phenyl and the aryl portion of aralkyl optionally substituted with 1 to 5 groups independently selected from the group consisting of : halo, C₁-4alkyl and C₁-4alkoxy, said C₁-4alkyl and C₁-4alkoxy optionally substituted with 1-3 halo groups,

25

or C is not present;

30 when C is not present then B is selected from the group consisting of: phenyl, C₅-16alkyl, C₅-16alkenyl, C₅-16alkynyl, -CHOH-C₄-15alkyl, -CHOH-C₄-15alkenyl, -

CHOH-C₄₋₁₅alkynyl, C₄₋₁₅alkoxy, -O-C₄₋₁₅alkenyl, -O-C₄₋₁₅alkynyl, C₄₋₁₅alkylthio, -S-C₄₋₁₅alkenyl, -S-C₄₋₁₅alkynyl, -CH₂-C₃₋₁₄alkoxy, -CH₂-O-C₃₋₁₄alkenyl, -CH₂-O-C₃₋₁₄alkynyl, -(C=O)-C₄₋₁₅alkyl, -(C=O)-C₄₋₁₅alkenyl, -(C=O)-C₄₋₁₅alkynyl, -(C=O)-O-C₃₋₁₄alkyl, -(C=O)-O-C₃₋₁₄alkenyl, -(C=O)-O-C₃₋₁₄alkynyl, -(C=O)-N(R₆)(R₇)-C₃₋₁₄alkyl, -(C=O)-N(R₆)(R₇)-C₃₋₁₄alkenyl, -(C=O)-N(R₆)(R₇)-C₃₋₁₄alkynyl, -N(R₆)(R₇)-(C=O)-C₃₋₁₄alkyl, -N(R₆)(R₇)-(C=O)-C₃₋₁₄alkenyl and -N(R₆)(R₇)-(C=O)-C₃₋₁₄alkynyl,

when **C** is phenyl or HET then **B** is selected from the group consisting of: C₁₋₆alkyl, C₁₋₅alkoxy, -(C=O)-C₁₋₅alkyl, -(C=O)-O-C₁₋₄alkyl, -(C=O)-N(R₆)(R₇)-C₁₋₄alkyl, -(C=O)-, -(CHOH)-, phenyl and HET, said phenyl and HET each optionally substituted from one up to the maximum number of substitutable positions with a substituent independently selected from the group consisting of: halo, phenyl, C₁₋₄alkyl, C₁₋₄alkoxy and aralkyl, said C₁₋₄alkyl and C₁₋₄alkoxy groups optionally substituted from one up to the maximum number of substitutable positions with a substituent independently selected from halo and hydroxy, and said phenyl and the aryl portion of aralkyl optionally substituted with 1 to 5 groups independently selected from the group consisting of : halo, C₁₋₄alkyl and C₁₋₄alkoxy, said C₁₋₄alkyl and C₁₋₄alkoxy optionally substituted with 1-3 halo groups, and

when **C** is C₁₋₈alkyl, C₁₋₈alkoxy, -(C=O)-C₁₋₆alkyl or -CHOH-C₁₋₆alkyl then **B** is phenyl or HET, said phenyl and HET each optionally substituted from one up to the maximum number of substitutable positions with a substituent independently selected from the group consisting of: halo, phenyl, C₁₋₄alkyl, C₁₋₄alkoxy and aralkyl, said C₁₋₄alkyl and C₁₋₄alkoxy groups optionally substituted from one up to the maximum number of substitutable positions with a substituent independently selected from halo and hydroxy, and said phenyl and the aryl portion of aralkyl optionally substituted with 1 to 5 groups independently selected from the group consisting of : halo, C₁₋₄alkyl and C₁₋₄alkoxy, said C₁₋₄alkyl and C₁₋₄alkoxy optionally substituted with 1-3 halo groups; and

R⁶ and R⁷ are independently selected from the group consisting of: hydrogen, C₁-9alkyl and -(CH₂)_q-phenyl, wherein q is 1 to 5 and phenyl is optionally substituted with 1-5 substituents independently selected from the group consisting of: C₁-3alkyl and C₁-3alkoxy, each optionally substituted with 1-3 halo groups.

5

2. The compound according to Claim 1 wherein:

Ar is phenyl and

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the group -B-C is attached to the phenyl ring at the 3- or 4-position.

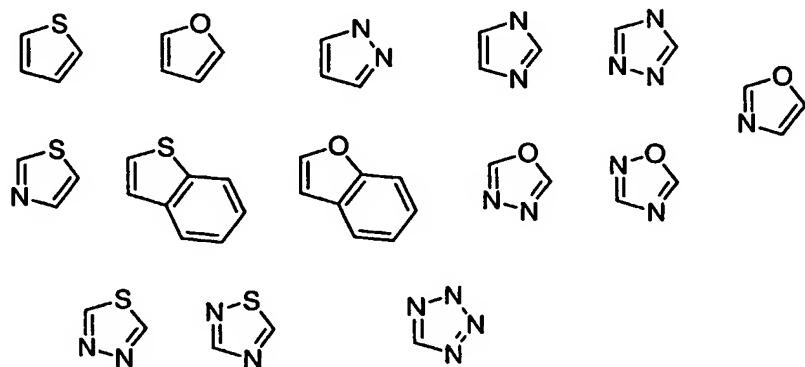
3. The compound according to Claim 1 wherein X is a bond, m is 2 and n is 2.

15

4. The compound according to Claim 1 wherein X is selected from O, NH or S, m is 1 and n is 2.

20

5. The compound according to Claim 1 wherein HET is selected from the group consisting of:



6. The method according to Claim 1 wherein **C** is not present and **B** is selected from the group consisting of: C₅-16alkyl, C₅-16alkenyl, C₅-16alkynyl, -CHOH-C₄-15alkyl, -CHOH-C₄-15alkenyl, -CHOH-C₄-15alkynyl, C₄-15alkoxy, -O-C₄-15alkenyl, -O-C₄-15alkynyl, C₄-15alkylthio, -S-C₄-15alkenyl, -S-C₄-15alkynyl, -CH₂-C₃-14alkoxy, -CH₂-O-C₃-14alkenyl, -CH₂-O-C₃-14alkynyl, -(C=O)-C₄-15alkyl, -(C=O)-C₄-15alkenyl, -(C=O)-C₄-15alkynyl, -(C=O)-O-C₃-14alkyl, -(C=O)-O-C₃-14alkenyl, -(C=O)-O-C₃-14alkynyl, -(C=O)-N(R⁶)(R⁷)-C₃-14alkyl, -(C=O)-N(R⁶)(R⁷)-C₃-14alkenyl, -(C=O)-N(R⁶)(R⁷)-C₃-14alkynyl, -N(R⁶)(R⁷)-(C=O)-C₃-14alkyl, -N(R⁶)(R⁷)-(C=O)-C₃-14alkenyl and -N(R⁶)(R⁷)-(C=O)-C₃-14alkynyl.

10

7. The compound according to Claim 1 wherein **C** is phenyl and **B** is selected from the group consisting of: C₁-6alkyl, C₁-5alkoxy, -(C=O)-C₁-5alkyl, -(C=O)-O-C₁-4alkyl and -(C=O)-N(R⁶)(R⁷)-C₁-4alkyl.

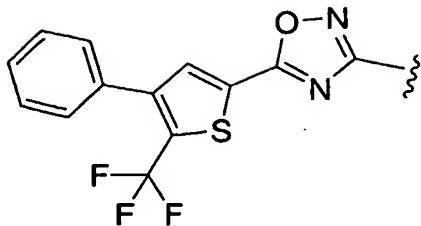
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8. The compound according to Claim 1 wherein:

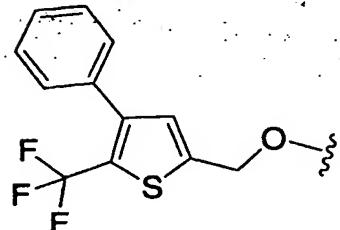
B-C is selected from the group consisting of:

20

- (1) **B** is C₇-10alkyl and **C** is not present,
- (2) **B** is C₆-9alkoxy and **C** is not present,
- (3) **B** is C₁-6alkyl or C₁-5alkoxy and **C** is phenyl, or
- (4) **B-C** is



or



9. A compound in accordance with Claim 1 wherein:

5

when X is a bond then m is 2 and n is 2,

when X is O, NH or S then m is 1 and n is 2,

10 Ar is phenyl and

the group -B-C is attached to the phenyl ring at the 3- or 4-position.

10. The compound in accordance with Claim 9 wherein C is not present and B is selected from the group consisting of: C₅-16alkyl, C₅-16alkenyl, C₅-16alkynyl, -CHOH-C₄-15alkyl, -CHOH-C₄-15alkenyl, -CHOH-C₄-15alkynyl, C₄-15alkoxy, -O-C₄-15alkenyl, -O-C₄-15alkynyl, C₄-15alkylthio, -S-C₄-15alkenyl, -S-C₄-15alkynyl, -CH₂-C₃-14alkoxy, -CH₂-O-C₃-14alkenyl, -CH₂-O-C₃-14alkynyl, -(C=O)-C₄-15alkyl, -(C=O)-C₄-15alkenyl, -(C=O)-C₄-15alkynyl, -(C=O)-O-C₃-14alkyl, -(C=O)-O-C₃-14alkenyl, -(C=O)-O-C₃-14alkynyl, -(C=O)-N(R⁶)(R⁷)-C₃-14alkyl,

14alkyl, -(C=O)-N(R⁶)(R⁷)-C₃-14alkenyl, -(C=O)-N(R⁶)(R⁷)-C₃-14alkynyl, -N(R⁶)(R⁷)-(C=O)-C₃-14alkyl, -N(R⁶)(R⁷)-(C=O)-C₃-14alkenyl and -N(R⁶)(R⁷)-(C=O)-C₃-14alkynyl.

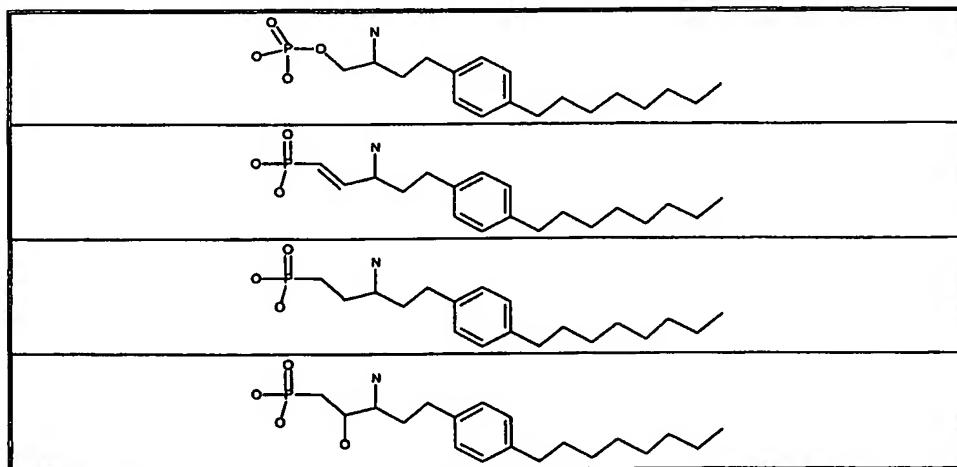
5 11. The compound in accordance with Claim 10 wherein **C** is not present and **B** is C₇-10alkyl.

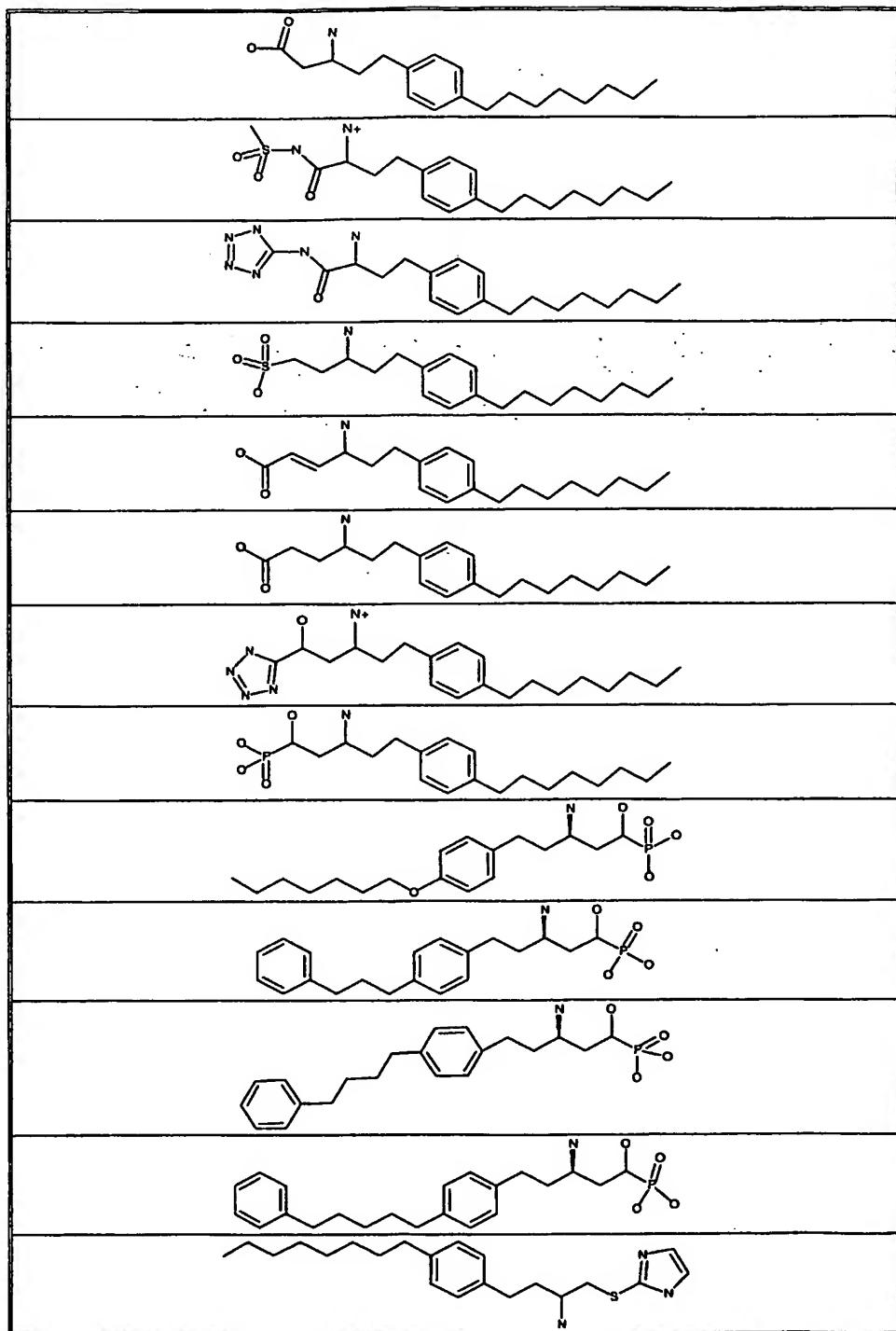
10 12. The compound in accordance with Claim 10 wherein **C** is not present and **B** is C₆-9alkoxy.

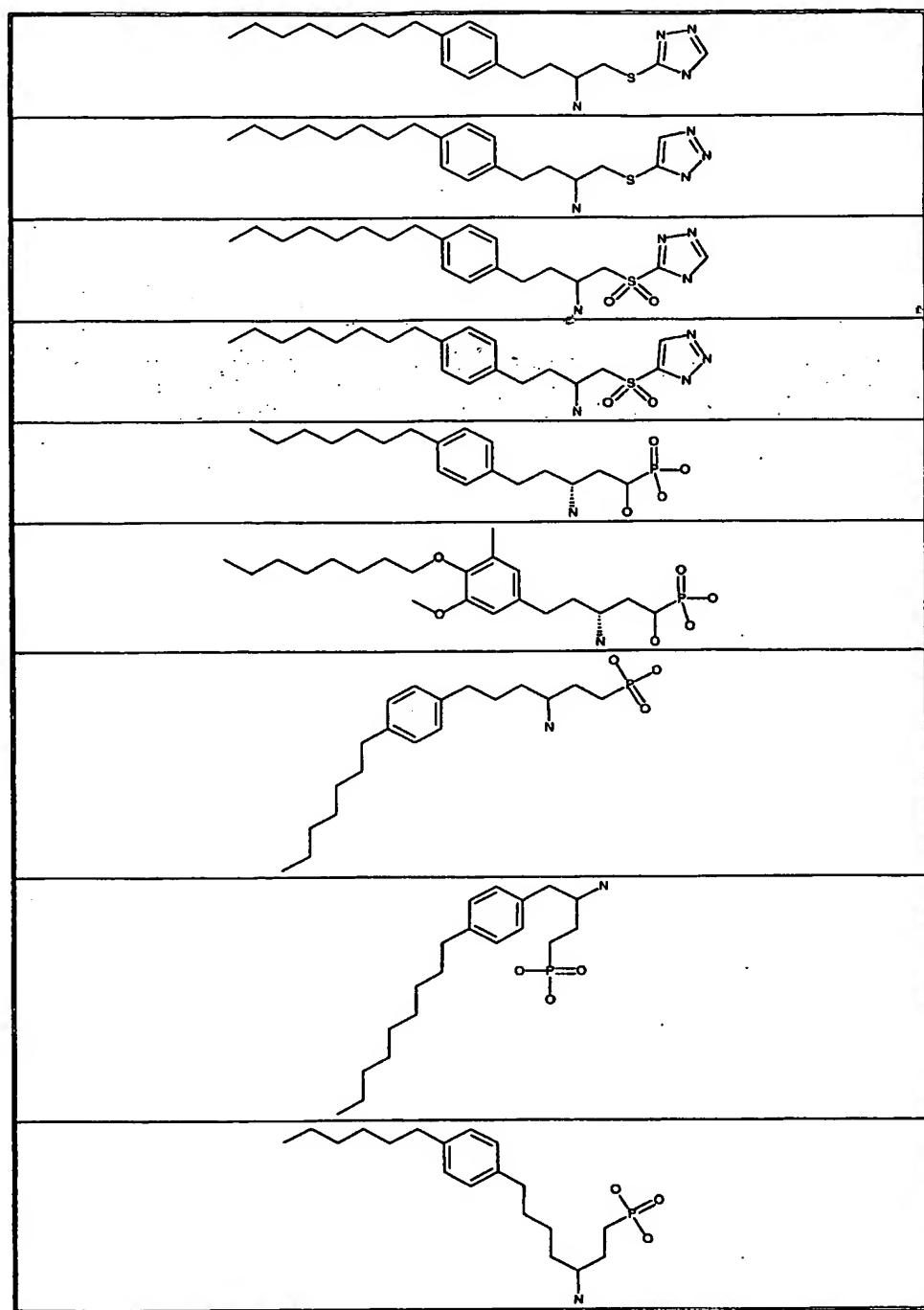
13. The compound in accordance with Claim 9 wherein **C** is phenyl and **B** is C₃-6alkyl.

14. The compound in accordance with Claim 9 wherein **A** is selected from the group consisting of: -CO₂H, -PO₃H₂, -PO₂H₂, -SO₃H and -PO(R⁸)OH.

20 15. A compound selected from the group consisting of:







16. A method of treating an immunoregulatory abnormality in a mammalian patient in need of such treatment comprising administering to said patient a compound in accordance with Claim 1 in an amount that is effective for treating said immunoregulatory abnormality.

5

17. The method according to Claim 16 wherein the immunoregulatory abnormality is an autoimmune or chronic inflammatory disease selected from the group consisting of: systemic lupus erythematosis, chronic rheumatoid arthritis, type I diabetes mellitus, inflammatory bowel disease, biliary 10 cirrhosis, uveitis, multiple sclerosis, Crohn's disease, ulcerative colitis, bullous pemphigoid, sarcoidosis, psoriasis, autoimmune myositis, Wegener's granulomatosis, ichthyosis, Graves ophthalmopathy and asthma.

18. The method according to Claim 16 wherein the 15 immunoregulatory abnormality is bone marrow or organ transplant rejection or graft-versus-host disease.

19. The method according to Claim 16 wherein the immunoregulatory abnormality is selected from the group consisting of: 20 transplantation of organs or tissue, graft-versus-host diseases brought about by transplantation, autoimmune syndromes including rheumatoid arthritis, systemic lupus erythematosus, Hashimoto's thyroiditis, multiple sclerosis, myasthenia gravis, type I diabetes, uveitis, posterior uveitis, allergic encephalomyelitis, glomerulonephritis, post-infectious autoimmune diseases including rheumatic fever and post-infectious 25 glomerulonephritis, inflammatory and hyperproliferative skin diseases, psoriasis, atopic dermatitis, contact dermatitis, eczematous dermatitis, seborrhoeic dermatitis, lichen planus, pemphigus, bullous pemphigoid, epidermolysis bullosa, urticaria, angioedemas, vasculitis, erythema, cutaneous eosinophilia, lupus erythematosus, acne, alopecia areata, keratoconjunctivitis, vernal conjunctivitis, uveitis associated with 30 Behcet's disease, keratitis, herpetic keratitis, conical cornea, dystrophia epithelialis cornea, corneal leukoma, ocular pemphigus, Mooren's ulcer, scleritis, Graves' ophthalmopathy, Vogt-Koyanagi-Harada syndrome, sarcoidosis, pollen allergies, reversible obstructive airway disease, bronchial asthma, allergic asthma, intrinsic

asthma, extrinsic asthma, dust asthma, chronic or inveterate asthma, late asthma and airway hyper-responsiveness, bronchitis, gastric ulcers, vascular damage caused by ischemic diseases and thrombosis, ischemic bowel diseases, inflammatory bowel diseases, necrotizing enterocolitis, intestinal lesions associated with thermal burns,

5 coeliac diseases, proctitis, eosinophilic gastroenteritis, mastocytosis, Crohn's disease, ulcerative colitis, migraine, rhinitis, eczema, interstitial nephritis, Goodpasture's syndrome, hemolytic-uremic syndrome, diabetic nephropathy, multiple myositis, Guillain-Barre syndrome, Meniere's disease, polyneuritis, multiple neuritis, mononeuritis, radiculopathy, hyperthyroidism, Basedow's disease, pure red cell

10 aplasia, aplastic anemia, hypoplastic anemia, idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia, agranulocytosis, pernicious anemia, megaloblastic anemia, anerythroplasia, osteoporosis, sarcoidosis, fibroid lung, idiopathic interstitial pneumonia, dermatomyositis, leukoderma vulgaris, ichthyosis vulgaris, photoallergic sensitivity, cutaneous T cell lymphoma, arteriosclerosis, atherosclerosis, aortitis

15 syndrome, polyarteritis nodosa, myocarditis, scleroderma, Wegener's granuloma, Sjogren's syndrome, adiposis, eosinophilic fascitis, lesions of gingiva, periodontium, alveolar bone, substantia ossea dentis, glomerulonephritis, male pattern alopecia or alopecia senilis by preventing epilation or providing hair germination and/or promoting hair generation and hair growth, muscular dystrophy, pyoderma and

20 Sezary's syndrome, Addison's disease, ischemia-reperfusion injury of organs which occurs upon preservation, transplantation or ischemic disease, endotoxin-shock, pseudomembranous colitis, colitis caused by drug or radiation, ischemic acute renal insufficiency, chronic renal insufficiency, toxinosis caused by lung-oxygen or drugs, lung cancer, pulmonary emphysema, cataracta, siderosis, retinitis pigmentosa, senile

25 macular degeneration, vitreal scarring, corneal alkali burn, dermatitis erythema multiforme, linear IgA ballous dermatitis and cement dermatitis, gingivitis, periodontitis, sepsis, pancreatitis, diseases caused by environmental pollution, aging, carcinogenesis, metastasis of carcinoma and hypobaropathy, disease caused by histamine or leukotriene-C₄ release, Behcet's disease, autoimmune hepatitis, primary

30 biliary cirrhosis, sclerosing cholangitis, partial liver resection, acute liver necrosis, necrosis caused by toxin, viral hepatitis, shock, or anoxia, B-virus hepatitis, non-A/non-B hepatitis, cirrhosis, alcoholic cirrhosis, hepatic failure, fulminant hepatic failure, late-onset hepatic failure, "acute-on-chronic" liver failure, augmentation of

chemotherapeutic effect, cytomegalovirus infection, HCMV infection, AIDS, cancer, senile dementia, trauma, and chronic bacterial infection.

20. The method according to Claim 16 wherein the
5 immunoregulatory abnormality is multiple sclerosis

21. The method according to Claim 16 wherein the
immunoregulatory abnormality is rheumatoid arthritis

10 22. The method according to Claim 16 wherein the
immunoregulatory abnormality is systemic lupus erythematosus

23. The method according to Claim 16 wherein the
immunoregulatory abnormality is psoriasis

15 24. The method according to Claim 16 wherein the
immunoregulatory abnormality is rejection of transplanted organ or tissue

20 25. The method according to Claim 16 wherein the
immunoregulatory abnormality is inflammatory bowel disease.

26. The method according to Claim 16 wherein the
immunoregulatory abnormality is a malignancy of lymphoid origin.

25 27. The method according to Claim 26 wherein the
immunoregulatory abnormality is acute and chronic lymphocytic leukemias and
lymphomas.

30 28. A method of suppressing the immune system in a mammalian
patient in need of immunosuppression comprising administering to said patient an
immunosuppressing effective amount of a compound of Claim 1.

29. A pharmaceutical composition comprised of a compound in accordance with Claim 1 in combination with a pharmaceutically acceptable carrier.